REMARKS

Upon entry of the present amendments, claims 18-34 are pending. Claims 3, 5, 7 and 8 are objected to. Claims 1-17 are rejected. Applicants have canceled claims 1-17.

New claims 18-34 have been added. Support for the newly submitted claims can be found in original claims 1-17 and in the specification as filed. The newly submitted claims add no new matter.

For the Examiner's convenience, a substitute specification is submitted herewith which incorporates all of the above amendments to the specification. The undersigned, a registered patent attorney, asserts that the substitute specification contains no new matter. A Verified Statement of the undersigned accompanies this Response. Applicants note, however, that page/line references in this Response are directed to the pages/lines in the originally filed specification.

The Examiner's rejections and objections are addressed in turn as set forth in the Office Action.

Oath/Declaration

The Office Action states that the oath or declaration is defection as incompliant with 37 CFR 1.67(a) because non-initialed and non-dated alterations have been made to the address of Gerard Grassy. To correct this, a newly executed declaration by all the inventors accompanies this response.

Informalities

The specification has been objected to for not conforming to 37 C.F.R. 1.822(d)(1) since the amino acids in the peptide sequences of the present invention are listed with one letter abbreviation instead of the required three-letter abbreviation with the first letter in upper case character. The Office Action requires correction.

Applicants traverse. Although Applicants have herein provided the amino acids with three-letter abbreviations, Applicants submit that the requirements of 37 C.F.R. 1.822(d)(1) apply **only** to the amino acids as recited in a Sequence Listing, not to the recitation of amino acids

within the specification. (emphasis added) *See* MPEP § 2429, wherein it is recited that "[s]ingle letter amino acid abbreviations are not acceptable within the Sequence Listing but may appear elsewhere in the application."

Claim Objections

Claims 3, 5, 7 and have been objected to for not conforming to 37 C.F.R. 1.822(d)(1) since the amino acids in the peptide sequences have been listed using one letter abbreviation. The Office Action recites that the use of three-letter format with the first letter as an upper case character is suggested.

Applicants have canceled claims 3, 5 and 7. The newly submitted claims all recite amino acids using three-letter format with the first letter as an upper case character, Applicants submit that the use of a one letter abbreviation is not incorrect as recited in MPEP § 2429, wherein it is recited that "[s]ingle letter amino acid abbreviations are not acceptable within the Sequence Listing but may appear elsewhere in the application."

In view of the submission of amended claims herein, Applicants submit that this objection is now moot and requests that it be withdrawn

Claims 3, 5, 7 and 8 are objected to because the claims contain "X", "B", "U" or "O" in the sequence, which should be "Xaa". The Office Action recites that the claims contain amino acid sequences, however, the sequence identifier "SEQ ID NO:" is not cited. The Office Action requests that each sequence be identified with a "SEQ ID NO:".

Claims 3, 5, 7 and 8 have been canceled. The newly submitted claims recite "Xaa" in the sequences instead of X", "B", "U" or "O". Additionally, the amino acid sequences in the newly submitted claims include a sequence identifier "SEQ ID NO:". In view of these amendments, Applicants submit that this objection is now moot and requests that it be withdrawn.

35 USC § 101

Claims 9 and 10 have been rejected under 35 U.S.C. § 101 because the claimed recitation of a use, without setting forth any steps involved in the process, i.e. results in a claim which is not a process under 35 U.S.C. § 101.

Claims 9 and 10 have been canceled. Newly submitted claim 20 corresponds to original claims 9 and 10 but is written in the proper form of a method claim and recites steps involved in the method. Accordingly, Applicants submit that new claim 20 is a proper method claim under35 U.S.C. § 101 and respectfully requests the withdrawal of this rejection.

35 USC § 112, first paragraph

Claims 1-17 have been rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for peptides of protegrin analog and of tachyplesin analogs shown in Tables I and II, which do not have disulfide bonds, conjugates of the peptide with doxorubicin or biotin, and the analogs of protegrin and tachyplesin as indicated in the prior art, does not reasonably provide enablement for all peptides derived from all antibiotic peptides, which do not have disulfide bond, a compound containing the peptide, an active substance and a signal agent, and a method of using the peptide to vector an active substance. According to the Office Action, the specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

As indicated on page 2, lines 6 to 12, protegrins and tachyplesins are β-stranded antibiotic peptides. Thus, the invention is directed to peptides derived from such β-stranded antibiotic peptides. This element has been added to the newly submitted claims.

Moreover, based on the description on page 7, lines 15 to 25, the absence of disulphide bonds in the peptides of the invention can be obtained by way of the removal of, the replacement by another amino acid or the blocking of the cysteine residues at their SH group level of all the cysteine residues, optionally except one. This element has been added to newly submitted claims. The addition of these elements in the new set of claims reduces the scope of the invention claimed and specifies that the present invention does not concern all kind of the antibiotic peptides.

Moreover, Applicants submit that there is more than adequate information in the present patent application to allow one skilled in the art to predict the internalization ability of a particular peptide. Based on the information disclosed from page 22, line 14 to page 23, line 2, one skilled in the art knows which amino acid can be changed to improve the internalization

ability. Alternatively, one skilled in the art can compare a peptide with an unknown internalization ability with the peptides disclosed in the patent application to have an idea of its internalization ability.

35 USC § 112, second paragraph

The Examiner has rejected claims 9 and 10 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The Examiner states that claims 9 and 10 provide for the use of a peptide obtained from an antibiotic peptide to vector active substances in an organism, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. According to the Office Action, a claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. The Office Action states that claims 9 and 10 are also indefinite as to "active substance", and that "it is not clear how the peptide vector the active substance, what is the active substance, and what function the active substance has."

Original claims 9 and 10 have been canceled. New claim 20 is a method claim that corresponds to the subject matter that was recited in original claims 9 and 10. New claim 20 properly recites a method for vectoring an active substance comprising β-stranded antibiotic peptide or an analog thereof. As submitted, new claim 20 recites steps which are a part of the claimed method. Additionally, the term "active substance" is defined in the specification on page 11, line 7 to page 12, line 13.

The Office Action recites that claims 1-8, 10 and 11 are indefinite because of the use of the term "derived from an antibiotic peptide or analog thereof". According to the Office Action, the term "derived from an antibiotic peptide or analog thereof" renders the claim indefinite, and it is unclear which peptide is intended as an antibiotic peptide, what amino acid sequence the analogs have, and what amino acid sequence the peptide has as compared to the parent "antibiotic peptide or an analog thereof".

Original claims 1-8, 10 and 11 have been canceled. New claim 18 incorporates the subject matter of original claim 1. New claim 18, however recites that the isolated peptide is derived from an antibiotic peptide or an analog thereof. The isolated peptide is devoid of a disulphide bond and has the amino acid sequence Arg-Arg-Leu-Ser-Tyr-Ser-Arg-Arg-Arg-Phe (SEQ ID NO:23). Furthermore, with regard to the phrase "derived from...", Applicants direct the Examiner's attention to the specification at page 8, lines 1-5. New claim 24 corresponds to original claim 11 and recites that A represents a linear peptide derived from a β-stranded antibiotic or an analog thereof, wherein the linear peptide is devoid of disulphide bonds. Applicants submit that the "derived from..." language in the newly submitted claims is clear and definite. It is thus submitted that the rejection to these claims under 35 U.S.C. § 112, second paragraph is now moot and should be withdrawn

The Office Action recites that claims 3-8, 10 and 17 are indefinite because of the use of the term "to any one of claims 1", "to one of claim 3", "to any of claim 1", or "to any claim 1". The term "to any of claims 1", "to one of claim 3", "to any of claim 1", or "to any claim 1" renders the claims indefinite because is it unclear regarding the dependency of the claim. Claims 3-8, 10 and 17 have been canceled from the present application. Newly submitted claims 18-34 have eliminated the indefinite language. It is submitted that the rejection to these claims under 35 U.S.C. § 112, second paragraph is now moot and should be withdrawn.

The Office Action recites that claim 3 recites the broad recitation "a succession of at least 5", and the claim also recites "preferably at least 7", which is the narrower statement of the range/limitation. Claim 3 is also indefinite because of the use of the term "at least", and it is not clear how many consecutive residues of formula (I) or (II) are in the peptide. Claim 11 recites the broad recitation "n is 0 or more" and "m is 1 or more", and the claims also recites "advantageously 0 or 1" and "preferably up to 10, advantageously up to 5", which is the narrower statement of the range/limitation. Claim 11 is also indefinite as to "n is 0 or more" and "m is 1 or more", and it is not clear what is the number of n or m?

Claims 3 and 11 have been canceled from the present application. Newly submitted claims 18-34 have eliminated the indefinite language. It is submitted that the rejection of claims 3 and 11 under 35 U.S.C. § 112, second paragraph is now moot and should be withdrawn.

The Office Action recites that claims 5 and 6 are indefinite because of the use of the terms "Aib" and "Abu". The terms "Aib" and "Abu" render the claim indefinite, and it is unclear what the term means. Claims 5 and 6 are also indefinite as to "[2-thienyl]alanine", as it is not clear whether the alanine has a the 2-thienyl group since the bracket indicates deletion, and the claim has alanine twice because of the deletion of 2-thienyl. Claim 6 is also indefinite because of the term "such as", since the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention.

Claims 5 and 6 have been canceled from the present application. Newly submitted claims 22, in part, and 23 correspond to original claims 5 and 6. The term "Aib" in new claim 22 has been corrected to recite its proper chemical name, amino isobutyric acid. The term "Abu" in new claim 23 has been corrected to recite its proper chemical name, amino butyric acid. Additionally, the term "[2-thienyl]alanine" has been corrected in new claims 22 and 23 to more properly recite β-(2-thienyl)alanine.

The Office Action states that claims 7 and 8 are indefinite because the claim contains non-elected sequences. Claims 7 and 8 have been canceled from the present application. The subject matter of original claims 7 and 8 has been incorporated into new claim18. New claim 18 recites the elected sequence of SEQ ID NO:23. The non-elected sequences have been deleted from the claim[s]. Applicants note that the present application had previously been subject to an election requirement wherein the sequence of SEQ ID NO:23 was elected with traverse.

Claims 11-17 have been held to be indefinite because of the use of the term "Z represents an active substance" or "Y represents a signal agent" renders the claims indefinite, and it is unclear what is the active substance, what function the active substance has, which peptide is signal agent, and which site the signal agent targets for.

Claims 11-17 have been canceled. The subject matter of original claims 11-17 is incorporated generally into newly submitted claims 25-34. Applicants direct the Examiner's attention to page 11, line 7 to page 12, line 13 wherein the definition of the term "active substance" is set forth. Additionally, the term "signal agent" is defined in the specification on page 12, line 27 to page 13, line 7.

Claim 13 has been deemed indefinite because of the use of the term "one or more covalent, hydrophobic or ionic bonds". The term "one or more covalent, hydrophobic or ionic bonds" renders the claim indefinite because is it unclear how many covalent, hydrophobic or ionic bonds are formed between peptide (A) and groups (Z) and (Y).

Claim 13 has been canceled from the present application. New claim 30 incorporates the subject matter of original claim 13. Support for the term "one or more covalent, hydrophobic or ionic bonds" can be found in the specification on page 13, line 8 to page 14, line 14.

The Office Action recites that claim 15 is indefinite because of the use of the terms "at least one signal agent (Y)" and "if present". The terms "at least one signal agent (Y)" and "if present" render the claim indefinite and it is unclear how many signal agents are in the compound, and whether or not the signal gent is present in the compound. See also claims 14, 16 and 17 regarding the term "at least".

Claim 15 has been canceled from the present application. New claim 32 incorporates the subject matter of original claim 15. New claim 32 has eliminated the phrase "if present".

The Office Action also recites that in claims 16 and 17 there is insufficient antecedent basis for the limitation "One compound of formula (TV)". Claims 16 and 17 have been canceled from the present application. New claims 33 and 34 incorporate the subject matter of original claims 16 and 17. The phrase "One compound of formula (TV)" recited in original claims 16 and 17has been corrected to recite "One compound of formula (IV)" in new claims 33 and 34. Antecedent basis is thus satisfied. It is submitted that the rejection of claims 16 and 17 under 35 U.S.C. § 112, second paragraph is now moot and should be withdrawn.

35 USC § 102

The Examiner has rejected claims 1-6 and 16 under 35 U.S.C. § 102(b) as allegedly anticipated by WO96/37508 to Lehrer *et al.*(hereafter "*Lehrer*"). Applicants respectfully traverse.

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. MPEP § 2131. "There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *Scripps Clinic & Research Foundation v. Genentech Inc.*, 18 USPQ 2d 1001, 1010 (Fed. Cir. 1991). Here, *Lehrer* does not disclose the claimed invention.

The Office Action recites that *Lehrer* teach various cationic antimicrobial and virus-neutralizing peptides obtained as protegrin analogs have no or one cysteine residue, where any of the 1-4 native cysteines are replaced with a hydrophobic or a small amino acid and various substituents (page 19, lines 35-38), which meets the criteria of claims 1-2. Peptides such as RGGRLAYARRRFAVAWGR is a sequence of formula (I), which meets the criteria of claims 3-5. Peptides which are referred to as "snake" forms of the compounds have all cysteines [that] are replaced by X, where X is a small amino acid, especially S and A (page 20, line 34-page 22, line 41), e.g., RGGRLXYXRRRFXVXVGR (Snake form-1), a sequence of formula (V), which meets the criteria of claim 6. Pharmaceutical composition of the peptides is used to inactivate a wide range of microorganisms including bacteria, yeast, protozoa and certain strain of virus (page 28, line 27-page 30, line 15), which meets the criteria of claim 6.

Claims 1-6 and 16 have been canceled. The rejection will be responded to with respect to the new claims as submitted herein. *Lehrer* discloses, pages 18 to 20, protegrin variants. None of these variants is a peptide devoid of disulphide bonds and which corresponds to the peptide of SEQ ID NO:23 disclosed in new claim 18. *Lehrer* does not teach the use of a β-stranded antibiotic peptide or an analogue thereof, wherein said peptide or analogue is devoid of disulphide bonds to vector active substances in an organism. Accordingly, new claim 18 and the claims that depend therefrom are not anticipated since *Lehrer* does not recite each and every element as set forth in new claim 18. Applicants respectfully request the withdrawal of this rejection.

The Examiner has rejected claims 1-2 and 16 under 35 U.S.C. § 102(b) as allegedly anticipated by Masuda *et al.,* Biochem. Biophys. Res. Comm. 189, 845-850 (1992) (hereafter "*Masuda*"). Applicants respectfully traverse as *Masuda* does not disclose the claimed invention.

The Office Action recites that *Masuda* teach a tachyplesin I analog, T10 (KWAFRVAYRGIAYRRAR-NH_2), in which all four cysteines are substituted with Ala, has no appreciable antiviral activity against HIV (page 847; FIG. 1, Table 1), which meets the criteria of claims 1-2 and 16.

Masuda discloses the antiviral activity against HIV type 1 of tachyplesin, polyphemusin and their analogs. None of these analogs correspond to the protegrin derivative peptide of SEQ ID NO:23 in new claim 18,.

Moreover, the article of *Masuda* neither discloses, nor suggests the use of a β-stranded antibiotic peptide or an analogue thereof, wherein said peptide or analogue is devoid of disulphide bonds to vector active substances in an organism. Accordingly, new claim 18 and the claims that depend therefrom are not anticipated since *Masuda* does not recite each and every element as set forth in new claim 18. Applicants respectfully request the withdrawal of this rejection.

The Examiner has rejected claims 1-2 and 16 under 35 U.S.C. § 102(b) as allegedly anticipated by Tamamura *et al.,* Chem. Pharm. Bill 41, 978-980 (1993) (hereafter "*Tamamura*"). Applicants respectfully traverse as *Tamamura* does not disclose the claimed invention. The Office Action recites that *Tamamura* teach a tachyplesin I analogs, 4-Ala-T-I, in which all four cysteines are substituted with Ala, and 4Cys(Acm)-T-I, where all cysteines are blocked, have decreased antibacterial activity (page 978; Fig. 1; Table 1), which meets the criteria of claims 1-2 and 16.

Tamamura concerns the study of the structure-anitimicrobial activity relationship of tachyplesin 1. Several tachyplesin 1 analogs were synthesized for these study but none of the

linear analogs (4Ala-T-1 and 4Cys(Avm)-T-1) corresponds to the peptides claimed in new claim 1 in the present patent application.

These linear analogs have been synthesized only to compare their antimicrobial activity with tachyplesin 1 activity and their use to vector active substances in an organism is not suggested. Furthermore, the tachyplesin 1 analogs described in *Tamamura* do not correspond to the protegrin derivative peptide of SEQ ID NO:23 in new claim 18 and the claims that depend therefrom. Accordingly, new claim 18 and the claims that depend therefrom are not anticipated since *Tamamura* does not recite each and every element as set forth in new claim 18. Applicants respectfully request the withdrawal of this rejection.

The Examiner has rejected claims 1-5 and 16 under 35 U.S.C. § 102(a) as allegedly anticipated by WO97/18826 to Chang *et al.*(hereafter "*Chang*"). Applicants respectfully traverse.

The Office Action recites that *Chang* teach an antimicrobial peptide, protegrin PC-8 (RGGRLAYARRRFAVAVGR), which is related to naturally-occurring protegrin peptides and does not have any cysteines, [and] has reduced inhibitory effect against *Neisseria gonorrhoeae* (page 75, lines 29-30; Table 17; Example 12), which meets the criteria of claims 1-5 and 16.

Chang discloses the protegrin 1 (PG-1) variant of the following formula RGGRLAYARRRFAVAVGR (PC-8) which is different from the peptide of new claim 18. Moreover, *Chang* neither discloses, nor suggests the use of said protegrin 1 (PG-1) variant devoid of disulphide bonds to vector active substances in an organism. Accordingly, new claim 18 and the claims that depend therefrom are not anticipated since *Chang* does not recite each and every element as set forth in new claim 18. Applicants respectfully request the withdrawal of this rejection.

The Examiner has rejected claims 1-5 and 16 under 35 U.S.C. § 102(a) as allegedly anticipated by Qu *et al.,* Infection and Immunity 65, 636-639 (February 1997) (hereafter "*Qu*"). Applicants respectfully traverse as *Qu* does not disclose the claimed invention. According to the Office Action, *Qu* teach an antimicrobial peptide, protegrin PC-8 (RGGRLAYARRRFAVAVGR), which is related to naturally-occurring protegrin peptides and does not have any cysteines, and has reduced inhibitory effects against *Neisseria gonorrhoeae* (pages 637-638; Table 1), which meets the criteria of claims 1-5 and 16.

Qu concerns a study of the antimicrobial activity of protegrin 1 (PG-1) variants, PG-1 containing 18 amino acid residues and having two intramolecular cystine disulphide bonds. One of these variants corresponds to RGGRLAYARRRFAVAVGR (PC-8) which is different from the peptide recited in new claim 18 of the present application.

The study in *Qu* provides evidence of the importance of the intramolecular disulphide bonds for the antimicrobial activity. Thus, with such a teaching, one skilled in the art will not synthetize other variants devoid of disulphise bonds. Moreover, *Qu*. neither discloses, nor suggests the use of said protegrin 1 (PG-1) variant devoid of disulphide bonds to vector active substances in an organism. Accordingly, new claim 18 and the claims that depend therefrom are not anticipated since *Qu* does not recite each and every element as set forth in new claim 18. Applicants respectfully request the withdrawal of this rejection.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**".

CONCLUSION

On the basis of the foregoing amendments, the points and concerns raised by the Examiner having been addressed in full, Applicants respectfully submit that the pending claims are in condition for allowance, which action is respectfully requested.

If, upon receipt and review of this amendment, the Examiner believes that the present application is not in condition for allowance and that changes can be suggested which would place the claims in allowable form, the Examiner is respectfully requested to call Applicant's undersigned counsel at the number provided below.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

***In the specification*:**

Please replace the paragraph beginning at page 4, line 17, with the following rewritten paragraph:

-- PG-1 : Arg-Gly-Gly-Arg-Leu-Cys-Tyr-Cys-Arg-Arg-Arg-Phe-Cys-Val-Cys-Val-Gly-Arg-NH_2 (SEQ ID NO: 1)

PG-2 : Arg-Gly-Gly-Arg-Leu-Cys-Tyr-Cys-Arg-Arg-Arg-Phe-Cys-Ile-Cys-Val-NH_2 (SEQ ID NO: 2)

PG-3 : Arg-Gly-Gly-Gly-Leu-Cys-Tyr-Cys-Arg-Arg-Arg-Phe-Cys-Val-Cys-Val-Gly-Arg-NH_2 (SEQ ID NO: 3)

PG-4 : Arg-Gly-Gly-Gly-Leu-Cys-Tyr-Cys-Arg-Gly-Trp-Ile-Cys-Phe-Cys-Val-Gly-Arg-NH_2 (SEQ ID NO: 4)

PG-5 : Arg-Gly-Gly-Gly-Leu-Cys-Tyr-Cys-Arg-Pro-Arg-Phe-Cys-Val-Cys-Val-Gly-Arg-NH_2 (SEQ ID NO: 5) --

Please replace line 30 on page 4, with the following rewritten line:

-- P1 : Arg-Arg-Trp-Cys-Phe-Arg-Val-Cys-Tyr-Arg-Gly-Phe-Cys-Tyr-Arg-Lys-Cys-Arg-NH_2 (SEQ ID NO: 6)--

Please replace lines 1-4 on page 5 with the following rewritten lines:

--P2 : Arg-Arg-Trp-Cys-Phe-Arg-Val-Cys-Tyr-Lys-Gly-Phey-Cys-Tyr-Arg-Lys-Cys-Arg-NH_2 (SEQ ID NO: 7)--

--T1 : Lys-Trp-Cys-Phe-Arg-Val-Cys-Tyr-Arg-Gly-Ile-Cys-Tyr-Arg-Arg-Cys-Arg-NH_2 (SEQ ID NO: 8)--

--T2 : Arg-Trp-Cys-Phe-Arg-Val-Cys-Tyr-Arg-Gly-Ile-Cys-Tyr-Arg-Lys-Cys-Arg-NH_2 (SEQ ID NO: 9)--

--T3 : Lys-Arg-Cys-Phe-Arg-Val-Cys-Tyr-Arg-Gly-Ile-Cys-Tyr-Lys-Arg-Cys-Arg-NH_2 (SEQ ID NO: 10)--

Please replace lines 21 -22 on page 8 with the following rewritten lines:

--Baa Xaa Xaa Baa Xaa Xaa Xaa Xaa Baa Baa Baa Xaa Xaa Xaa Xaa Xaa Xaa Baa (I) (SEQ ID NO: 11)

Baa Baa Xaa Xaa Xaa Baa Xaa Xaa Xaa Baa Xaa Xaa Xaa Xaa Baa Baa Xaa Baa (II) (SEQ ID NO: 12)--

Please replace line 25 on page 8 with the following rewritten line:

--Baa (Xaa Baa) Xaa (Xaa Baa) Xaa (Xaa Baa) Xaa Xaa (Xaa Baa) Baa (Xaa Baa)Xaa Xaa Xaa (Xaa Baa) (Xaa Baa) Xaa Baa (SEQ ID NO : 38)--

Please replace the paragraph starting at line 27 on page 8 with the following rewritten paragraph:

-- - the Baa groups, identical or different, represent an amino acid residue whose side chain carries a base group, and--

Please replace the paragraph starting at line 30 on page 8 with the following rewritten paragraph:

-- - the Xaa groups, identical or different , represent an aliphatic or aromatic amino acid residue,--

Please replace the paragraph starting at line 6 on page 9 with the following rewritten paragraph:

--Baa and Xaa may or may not be natural amino acids, including D-amino acids--

Please replace the paragraph starting at line 10 on page 9 with the following rewritten paragraph:

--Baa is chosen from among arginine, lysine, diaminoacetic acid, diaminobutyric acid, diaminoproprionic acid, ornithine.--

Paragraph beginning at line 13 on page 9 has been amended as follows:

-- Xaa is chosen from among glycine, alanine, valine, norleucine, isoleucine, leucine, cysteine, cysteine^{Acm}, penicillamine, methionine, serine, threonine, asparagine, glutamine, phenylalanine, histidine, tryptophan, tyrosine, proline, [Abu] Amino butyric acid, carboxylic amino-1-cyclohexane acid, [Aib] Amino isobutyric acid, carboxylic 2-aminotetraline, 4-bromophenylalanine, tert-Leucine, 4-chlorophenylalanine, β-cyclohexylalanine, 3,4-dichlorophenylalanine, 4-fluorophenylalanine, homoleucine, β-homoleucine, homophenylalanine, 4-methylphenylalanine, 1-naphthylalanine, 2-naphthylalanine, 4-nitrophenylalanine, 3-nitrotyrosine, norvaline, phenylglycine, 3-pyridylalanine, [[2-Thienyl]-alanine] (2-Thienyl)-alanine.

Please replace lines 4-5 on page 10 with the following rewritten lines:

--Arg Xaa Xaa Arg Xaa Uaa Xaa Uaa Arg Arg Arg Xaa Uaa Xaa Uaa Xaa Xaa Arg -NH_2 (V) (SEQ ID NO : 13)

Arg Arg Xaa Uaa Xaa Arg Xaa Uaa Xaa Arg Xaa Xaa Uaa Xaa Arg Arg Uaa Arg -NH_2 (VI) (SEQ ID NO : 14)--

Please replace line 7 on page 10 with the following rewritten line:

-- Uaa represents serine or threonine--

Please delete line 8 on page 10.

Paragraph beginning at line 9 on page 10 has been amended as follows:

--the Xaa groups, identical or different, represent an amino acid which may or may not be natural (including D-amino acids), either aliphatic or aromatic, such as among glycine, alanine, valine, norleucine, isoleucine, leucine, cysteine, cysteine^{Acm}, penicillamine, methionine, serine, threonine, asparagine, glutamine, phenylalanine, histidine, tryptophan, tyrosine, proline, [Abu] Amino butyric acid, carboxylic amino-1-cyclohexane acid, [Aib] Amino isobutyric acid, carboxylic 2-aminotetraline, 4-bromophenylalanine, tert-Leucine, 4-chlorophenylalanine, β-cyclohexylalanine, 3,4-dichlorophenylalanine, 4-fluorophenylalanine, homoleucine, β-homoleucine, homophenylalanine, 4-methylphenylalanine, 1-naphthylalanine, 2-naphthylalanine, 4-nitrophenylalanine, 3-nitrotyrosine, norvaline, phenylglycine, 3-pyridylalanine, [[2-Thienyl]-alanine] (2-Thienyl)-alanine.--

Please replace Table I on page 11 as follows:

--

Code	Sequence	Modification
SM1738	Arg-Gly-Gly-Arg-Leu-Ser-Tyr-Ser-Arg-Arg-Arg-Phe-Ser-Val-Ser-Val-Gly-Arg (SEQ ID NO:15)	Head of series
SM1736	arg-gly-gly-arg-leu-ser-tyr-ser-arg-arg-arg-phe-ser-val-ser-val-gly-arg (SEQ ID NO:15)	Amino acid of D form of SM1738
SM1727	Arg-Gly-Val-Ser-Val-Ser-Phe-Arg-Arg-Arg-Ser-Tyr-Ser-Leu-Arg-Gly-Gly-Arg (SEQ ID NO:17)	Retro form of SM1738
SM1739	Glu-Gly-Gly-Glu-Leu-Ser-Tyr-Ser-Glu-Glu-Glu-Phe-Ser-Val-Ser-Val-Gly-Glu (SEQ ID NO:18)	Reversed Charge (R → E)
SM2187	Arg-Gly-Gly-Arg-Leu-Ala-Tyr-Arg-Leu-Leu-Arg-Phe-Ala-Ile-Arg-Val-Gly-Arg (SEQ ID NO:19)	Increased amphipathicity
SM2188	Oaa-Gly-Gly-Oaa-Xaa-Xaa-Baa-Oaa-Xaa-Xaa-Oaa-Baa-Xaa-Xaa-Xaa-Oaa-Xaa-Gly (SEQ ID NO:20)	Increased hydrophobicity
SM2189	Arg-Ala-Ala-Arg-Leu-Gly-Tyr-Arg-Xaa-Xaa-Arg-Phe-Gly-Zaa-Arg-Val-Gly-Arg (SEQ ID NO:21)	Increased amphipathicity
SM2194	Tyr-Arg-Arg-Arg-Phe-Ser-Val-Ser-Val-Arg (SEQ ID NO:22)	C-terminal end of SM2193
SM2195	Arg-Arg-Leu-Ser-Tyr-Ser-Arg-Arg-Arg-Phe (SEQ ID NO:23)	N-terminal end of SM2193
SM2193	Arg-Arg-Leu-Ser-Tyr-Ser-Arg-Arg-Arg-Phe-Ser-Val-Ser-Val-Arg (SEQ ID NO:24)	Reduced flexibility (G deletion)
SM2196	Arg-Gly-Gly-Arg-Leu-Ser-Tyr-Ser-Arg-Arg-Arg-Phe-Ser-Thr-Ser-Thr-Gly-Arg (SEQ ID NO:25)	Inhibition dimerization

--.

Please replace Table II on page 11 as follows:

--

Code	Sequence	Modification
SM1726	Lys-Trp-Ser-Phe-Arg-Val-Ser-Tyr-Arg-Gly-Ile-Ser-Tyr-Arg-Arg-Ser-Arg (SEQ ID NO:26)	Head of series
SM2307	Arg-Trp-Ser-Phe-Arg-Val-Ser-Tyr-Arg-Gly-Ile-Ser-Tyr-Arg-Arg-Ser-Arg (SEQ ID NO:27)	K → R mutation
SM2392	arg-trp-ser-phe-arg-val-ser-tyr-arg-gly-ile-ser-tyr-arg-arg-ser-arg (SEQ ID NO:28)	Amino acid of D form (of SM2307)

SM2309	lys-trp-ser-phe-arg-val-ser-tyr-arg-gly-ile-ser-tyr-arg-arg-ser-arg (SEQ ID NO:29)	Amino acid of D form (of SM1726)
SM2310	Arg-Ser-Arg-Arg-Tyr-Ser-Ile-Gly-Arg-Tyr-Ser-Val-Arg-Phe-Ser-Trp-Lys (SEQ ID NO: 30)	Retro form
SM2190	Oaa-Baa-Xaa-Baa-Oaa-Xaa-Xaa-Baa-Oaa-Gly-Xaa-Oaa-Baa-Xaa-Xaa-Oaa-Xaa (SEQ ID NO:31)	Increased hydrophobicity
SM2191	Lys-Trp-Ala-Phe-Arg-Val-Ala-Tyr-Arg-Gly-Ile-Arg-Tyr-Leu-Leu-Arg-Leu (SEQ ID NO:32)	Increased amphipathicity
SM2192	Lys-Tyr-Ala-Trp-Arg-Val-Ala-His-Arg-Gly-Ile-Arg-Trp-Leu-Leu-Arg-Xaa (SEQ ID NO:33)	Increased amphipathicity

Please replace the paragraph beginning at line 4 on page 11 with the following rewritten paragraph:

--In the sequences of tables I and II above, Baa represents Naphthylalanine, Oaa represents Ornithine, Xaa represents Norleucine and Zaa represents Norvaline.

On page 12, line 9, after "etc.", please delete "..".

Please replace the sentence at page 12, line 25, with the following rewritten sentence:

-- - m is 1 or more, preferably [up] m is 1 to 10, [advantageously up] more preferably m is 1 to 5.--

Please replace lines 6-8 on page 17 with the following rewritten lines:

-- Arg-Gly-Gly-Arg-Leu-Xaa-Tyr-Xaa-Arg-Arg-Arg-F-Xaa-Val-Xaa-Val-Gly-Arg-NH_2 (SEQ ID NO:34)--

-- Arg-Arg-Trp-Xaa-Phe-Arg-Val-Xaa-Tyr-Arg-Gly-Phe-Xaa-Tyr-Arg-Lys-Xaa-Arg-NH_2 (SEQ ID NO:35)--

-- Lys-Trp-Xaa-Ph-Arg-Val-Xaa-Tyr-Arg-Gly-Ile-Xaa-Tyr-Arg-Arg-Xaa-Arg-NH_2 (SEQ ID NO:36)--

Please replace line 13 on page 17 with the following rewritten line:

-- Arg-Gly-Gly-Arg-Leu-CysTyr-Cys-Arg-Arg-Arg-Phe-Cys-Val-Cys-Val-Gly-Arg-NH_2 (SEQ ID NO:1)--

Please replace line 15 on page 17 with the following rewritten line:

-- Lys-Trp-Cys-Phe-Arg-Val-Cys-Tyr-Arg-Gly-Ile-Cys-Tyr-Arg-Arg-Cys-Arg-NH_2 (SEQ ID NO: 8)--

Please replace line 17 on page 17 with the following rewritten line:

-- Lys Trp Xaa Phe Arg Val Xaa Tyr Arg Gly Ile Xaa Tyr Arg Arg Xaa Arg-NH_2 (SEQ ID NO:36)--

Please replace line 8 on page 18 with the following rewritten line:

-- Arg-Gly-Gly-Arg-Leu-Xaa-Tyr-Xaa-Arg-Arg-Arg-Phe-Xaa-Val-Xaa-Val-Gly-Arg-NH_2 (SEQ ID NO:37)--

Line 25 on page 19 has been amended as follows:

--[R] Arg -[X] Xaa -[X] Xaa -[R] Arg -[X] Xaa -[U] Uaa-[X] Xaa -[U] Uaa-[R] Arg -[R] Arg -[R] Arg -[X] Xaa -[U] Uaa-[X] Xaa -[U] Uaa-[X] Xaa -[X] Xaa -[R] Arg -NH_2 (SEQ ID NO:13)--

Line 26 on page 19 has been amended as follows:

--[R] Arg-[R] Arg -[X] Xaa-[U] Uaa-[X] Xaa -[R] Arg -[X] Xaa -[U] Uaa--[X] Xaa -[R] Arg -[X] Xaa -[X] Xaa -[U] Uaa--[X] Xaa -[R] Arg -[R] Arg -[U] Uaa--[R] Arg -NH_2 (SEQ ID NO:14)--

Paragraph beginning at line 1 on page 20 has been amended as follows:

the Xaa groups, identical or different, represent an amino acid which may or may not be natural (including D-amino acids), either aliphatic or aromatic, such as among glycine, alanine, valine, norleucine, isoleucine, leucine, cysteine, cysteine^{Acm}, penicillamine, methionine, serine, threonine, asparagine, glutamine, phenylalanine, histidine, tryptophan, tyrosine, proline, [Abu] Amino butyric acid, carboxylic amino-1-cyclohexane acid, [Aib] Amino isobutyric acid, carboxylic 2-aminotetraline, 4-bromophenylalanine, tert-Leucine, 4-chlorophenylalanine, β-cyclohexylalanine, 3,4-dichlorophenylalanine, 4-fluorophenylalanine, homoleucine, β-homoleucine, homophenylalanine, 4-methylphenylalanine, 1-naphthylalanine, 2-naphthylalanine, 4-nitrophenylalanine, 3-nitrotyrosine, norvaline, phenylglycine, 3-pyridylalanine, [[2-Thienyl]-alanine] (2-Thienyl)-alanine.

In the claims:

Claims 1-17 have been canceled

New claims 18-34 are submitted herein.